REMARKS

The Final Office action dated July 31, 2007 is acknowledged. Claims 1-6 and 8-16 are pending in the instant application. According to the Office action, each of claims 1-6 and 8-16 has been rejected. By the present Office Action response, claim 1 has been amended, claims 11, 14 and 15 have been canceled and claims 17 and 18 have been added. It is noted that the subject matter of canceled claim 11 has been incorporated into independent claim 1. Moreover, new claims 17 and 18 are substantially based on canceled claims 14 and 15, support for which may be found in the specification, such as in the "Examples," for example paragraph [000050].

The Applicant wishes to thank the Examiner for the withdrawal of the previous claim objection and rejection under Section 102(a) and (e). Reconsideration of the present rejection is respectfully requested in light of the amendments being made hereby and the arguments made herein. No new matter has been added.

Claim Objections

The Examiner has objected to claims 14 and 15 as being "use" claims. Claims 14 and 15 have been canceled. Therefore, this objection is no longer germane. Withdrawal thereof is respectfully requested.

Rejection of Claims 1-6 and 8-16 Under 35 U.S.C. 103(a)

Claims 1-6 and 8-16 have been rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,444,234 (Kirby, et al.), taken with U.S. Patent No. 5,759,445 (Yamamoto, et al.), Guo, et al. (Drug Deli. Vol. 7, No. 2, pp. 113-116, 2000) and Thorand, et al. (Southeast Asian J. Trop. Med. Public Health, Vol. 24, No. 4, pp. 624-630, 1993).

The Examiner states that the primary reference of Kirby, et al. discloses a composition for transdermal administration of at least one therapeutically active compound (i.e., polypeptide) or nutrient (i.e., vitamins) comprising one item selected from the group consisting of at least one therapeutically active compound such as antibiotic drugs and least one nutrient and a non-oily emulsion (cholesterol), wherein the polypeptide has a molecular weight of 500 D and higher (which overlaps with the range of up to 7000 kDA of claim 5) and further comprising an organic sulfur compound (methylsulfonylmethane), wherein the composition for transdermal administration of active substance which is nutrients and/or medications are useful as a cream, gel, lotion, ointment and patch. The Examiner also acknowledges that the Kirby, et al. patent differs from the presently claimed invention by not teaching the use of a non-oily emulsion which is a mixture of lecithin, bile salt and cholesterol with the specific ratio and amount disclosed in the present claims and the use of a nutrient which is an ionic compound and where the ionic compound is a metal ion. However, the Examiner states that Guo, et al. teach a study of transdermal delivery of insulin (therapeutically active compound and/or peptide) in mice by using lecithin vesicles as a carrier and disclose that flexible vesicles may become a promising carrier for transdermal delivery of hydrophilic polypeptides.

In addition, the Examiner states that Yamamoto, et al. teach an aqueous dispersed solution which comprises the steps of evaporating an organic solvent from a mixture prepared by adding cholesterol, lecithin, a surfactant and a neutral lipid, and/or a cholesterol ester in the organic solvent in a specific range of the concentration ratio. The Examiner concludes that by utilizing the mixtures of non-oily emulsion of lecithin, bile salt and cholesterol is a choice procedure (per Yamamoto, et al.) and is therefore obvious

to one of ordinary skill in the art since it is reasonably expected that use of a non-oily emulsion, such as lecithin, would have resulted as a promising carrier for transdermal delivery of hydrophilic polypeptides as taught by Guo, et al. Therefore, according to the Examiner, one skilled in the art would have been motivated to employ a composition for transdermal administration of the primary reference because such features are known or suggested in the art, in order to arrive at the presently claimed invention.

Regarding Thorand, et al., the Examiner states that the reference demonstrates that the administration of iron (metal ion) supplement is an effective intervention in treating anemia caused by iron deficiency. Thus, the Examiner concludes that the reference shows the administration of at least one therapeutically active compound, wherein the at least one nutrient is an ionic compound and wherein the ionic compound is a metal ion (i.e., iron as a nutrient) to meet the limitations of present claims 2 and 3.

The Examiner thus concludes that it would have been obvious to combine the teachings of the aforementioned references to arrive at the presently claimed invention.

The Applicant respectfully submits that to establish a *prima facie* case of obviousness, three basic criteria must be met, as set forth in M.P.E.P. § 2142. First, there must be some suggestion or motivation to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The Applicant respectfully disagrees with the Examiner's conclusion set forth in the Office action. However, in response to the Examiner's rejection, the Applicant has amended claim 1 from having "open-ended" language (i.e., "comprising") to "closed

language" (i.e., "consisting of").

As noted in the previous Office action response, the present invention provides therapeutically active polypeptides or ionic nutrients administered through the human skin if a non-oily emulsion of lecithin, bile salts and cholesterol in water is utilized and that despite considerable effort, such an invention simply has not yet been achieved. In particular, the prior art has not yet achieved providing a reliable system for transdermal administration of polypeptides or ions which would enable transdermal administration of insulin to a diabetic patient at a therapeutically sufficient rate and without providing a risk of hypoglycemia, as noted in paragraph [000029] (and elsewhere) of the present specification. The present invention may provide the basis for a system by which numerous diabetic patients would benefit. The presently claimed invention achieves this goal. In short, the prior art fails to teach or make obvious the utility of a non-oily emulsion which is a mixture of lecithin, bile salts and cholesterol in water.

It is submitted that present claim 1, as amended, excludes the presence of a source of cellular activation energy from the claimed composition. To the contrary, the source of cellular activation energy is essentially required in accordance with Kirby, et al. As noted in the earlier response, a crucial aspect of the formulation of Kirby, et al. is the presence of Foskolin or other source of cellular energy (D), namely, induction of cAMP or cGMP (Abstract). The source of cellular activation energy may be selected from the group consisting of ATP (claim 1), ADP, NADH, and $FADH_2$ (col. 12, lines 39-42), Forskolin, Colforsin and coleonol (col. 12, lines 52-57), methyl xanthines, Saikogenin, Saikosaponin, *Angelacie dahuricae* radix, phelopterin, oxypeucedanin, acetylcholine, cytidene, diphosphocholine and ascorbic acid (Vitamin C) (col. 12, lines 58-65). The

source of cellular activation energy shall minimize energy-negative reactions which could lead to sensitization, ACD or anaphylaxis (col, 12, lines 28-35). Thus, is should be apparent to one skilled in the art from the disclosure of Kirby, et al. in col. 6, lines 20-30; col. 6, line 66 – col. 7, line 18; col. 7, lines 22-47; col. 9, lines 43-45 and claim 1 that the source of cellular activation energy is an essential component of the liquid carrier composition for the transdermal delivery of a medicament, as disclosed therein. Thus, it is submitted that the teaching of Kirby, et al. pertains to an active method of transdermal drug delivery, while the present invention concerns passive transdermal delivery of a therapeutically active ingredient or nutrient. Moreover, it is respectfully submitted that Guo, et al., Yamamoto, et al. and Thorand, et al. all fail to make up for any deficiencies of Kirby, et al. and fail to provide a reasonable expectation of success.

To summarize, it is respectfully submitted that the presently claimed invention is not rendered obvious by the combination of teachings of the prior art since because such combined teachings (i.e., Kirby, et al. taken with Yamamoto, et al., Guo, et al. and Thorand, et al.) would still always lead to a composition that contains a source of cellular activation energy. Moreover, none of the cited prior art teach or suggest that the energy of cellular activation energy can be omitted without impairing the transdermal delivery of the pharmaceutically active agents. In turn, a composition for transdermal administration of a therapeutically active compound or nutrient which consists of at least one therapeutically active compound or at least one nutrient, a non-oily emulsion which is a mixture of lecithin, bile salts and cholesterol in water, and an optional organic sulfur compound is clearly novel and not rendered obvious in view of the prior art.

It is therefore respectfully submitted that the present invention defined in the

presently amended claims is patentably distinguishable over the combination of prior art teachings under 35 U.S.C. 103(a). Based on the aforementioned differences, each and every element of the present invention recited in claims 1-6 and 8-16 are not set forth in the Kirby, et al., alone or in combination with any of the cited secondary references. Moreover, one skilled in the art would not be motivated to combine said references or to modify Kirby, et al. to arrive at the presently claimed invention. Even if one were to do so, there would be no expectation of success. Therefore, the Applicant respectfully requests that this rejection be withdrawn.

Conclusion

For the foregoing reasons, it is believed that the present application, as amended, is in condition for allowance, and such action is earnestly solicited. Based on the foregoing arguments, amendments to the claims and deficiencies of the prior art references, the Applicant strongly urges that the obviousness-type rejection and anticipation rejection be withdrawn. The Examiner is invited to call the undersigned if there are any remaining issues to be discussed which could expedite the prosecution of the present application.

Respectfully submitted,

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